

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/012989

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K45/06 A61K31/4025 A61K31/40 A61K31/401 A61P3/00
A61P9/00 A61P17/00 A61P27/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EP0-Internal, PAJ, WPI Data, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/183367 A1 (SULSKY RICHARD B ET AL) 5 December 2002 (2002-12-05) paragraphs [0002], [0022], [0025], [0124], [0126], [0127] claims 12,17,18	1-3,6-9, 11,16
X	----- WO 01/68603 A (BRISTOL-MYERS SQUIBB CO; ROBL, JEFFREY, A; SULSKY, RICHARD, B; AUGERI,) 20 September 2001 (2001-09-20) page 1, paragraph 1 page 6, paragraph 1 page 29, line 36 - page 31, line 3 ----- -/--	1-3,6-9, 11,16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the International filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

20 June 2005

Date of mailing of the international search report

13. 10. 2005

Name and mailing address of the ISA

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PCT/EP2004/012989

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/000181 A (MERCK & CO., INC; BROCKUNIER, LINDA; PARMEE, EMMA; WEBER, ANN, E) 3 January 2003 (2003-01-03) page 1, line 5 - line 10 page 21, line 25 - line 27 claims 1,25,34 -----	1-3,6-9, 11,16
X	WO 02/083128 A (BRISTOL-MYERS SQUIBB COMPANY; SULSKY, RICHARD, B; ROBL, JEFFREY, A) 24 October 2002 (2002-10-24) page 1, paragraph 1 page 29 claims 12,17,18 -----	1-3,6-9, 11,16
X	WO 02/076450 A (MERCK & CO., INC; ASHTON, WALLACE, T; CALDWELL, CHARLES, G; OK, HYUN;) 3 October 2002 (2002-10-03) page 3, line 21 - line 27 page 24, line 16 - line 34 page 25, line 30 - page 32 -----	1-3,6-9, 11,16
X	WO 03/082817 A (MERCK & CO., INC; BROCKUNIER, LINDA, L; DUFFY, JOSEPH, L; KIM, DOOSEOP) 9 October 2003 (2003-10-09) page 3, line 23 - line 29 page 22, line 13 - line 32 page 24, paragraph 1 -----	1-3,6-9, 11,16
Y	WO 02/083109 A (FERRING BV; BROQUA, PIERRE; SUDRE, BEATRICE; AUBERT, MICHEL, L) 24 October 2002 (2002-10-24) example 1D claim 1 -----	1-16
Y	HUGHES T.E. ET AL: "NVP- DPP728 (1-[[[2-[(5-cyanopyridin-2-yl)amino]ethyl] amino] acetyl]-2- cyano-(S)-pyrrolidine), a slow-binding inhibitor of dipeptidyl peptidase IV." BIOCHEMISTRY, VOL. 38, NO. 36, PP. 11597-11603. REFS: 31 ISSN: 0006-2960 CODEN: BICHAW, 7 September 1999 (1999-09-07), XP000983860 abstract -----	1-16
Y	SCHEEN A J ET AL: "ANTI OBESITY PHARMACOTHERAPY IN THE MANAGEMENT OF TYPE 2 DIABETES" DIABETES/METABOLISM RESEARCH AND REVIEWS, WILEY, LONDON,, GB, vol. 16, no. 2, March 2000 (2000-03), pages 114-124, XP009001875 ISSN: 1520-7552 abstract -----	1-16

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Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 7, 10-12 and 16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
invention 1: claims 1-16 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, delay of progression or treatment of type 2 diabetes mellitus

Invention 2: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, delay of progression or treatment of insulin resistance and syndrome X and obesity, as far as not included in the subject of the previous invention.

Invention 3: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, delay of progression or treatment of hypertension including hypertension in the elderly, familial dyslipidemic hypertension, and isolated systolic hypertension (ISH); increased collagen formation, fibrosis, and remodeling following hypertension; erectile dysfunction, impaired vascular compliance, stroke; all these diseases or conditions associated with or without hypertension, as far as not included in the subject of one of the previous inventions.

Invention 4: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, delay of progression or treatment of congestive heart failure, left ventricular hypertrophy, survival post myocardial infarction (MI), coronary artery diseases, atherosclerosis, angina pectoris, thrombosis, as far as not included in the subject of one of the previous inventions.

Invention 5: claims 1-16 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of renal failure, especially chronic renal failure, glomerulosclerosis, nephropathy, as far as not included in the subject of one of the previous inventions.

Invention 6: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of hypothyroidism, as far as not included in the subject of one of the previous inventions.

Invention 7: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of endothelial dysfunction with or without hypertension, as far as not included in the subject of one of the previous inventions.

Invention 8: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of hyperlipidemia, hyperlipoproteinemia, hypertryglyceridemia, and hypercholesterolemia, as far as not included in the subject of one of the previous inventions.

Invention 9: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of macular degeneration, cataract, glaucoma, as far as not included in the subject of one of the previous inventions.

Invention 10: claims 1-16 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of skin and connective tissue disorders, as far as not included in the subject of one of the previous inventions.

Invention 11: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of restenosis after percutaneous transluminal angioplasty, and restenosis after coronary artery bypass surgery, as far as not included in the subject of one of the previous inventions.

Invention 12: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino] ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention or delay of progression or treatment of peripheral vascular disease, as far as not included in the subject of one of the previous inventions.

Inventions 13-24: claims 1-16 (all partially)

A combination comprising 1(S)-1-[(3-hydroxy-1-adamantyl) amino]acetyl-2-cyano-pyrrolidine and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 13, the one of invention 2 for invention 14, and so on to the one of invention 12 for invention 24, as far as not included in the subject of one of the previous inventions.

Inventions 25-36: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising L-threo- isoleucylthiazolidine and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 25, the one of invention 2 for invention 26, and so on to the one of invention 12 for invention 36, as far as not included in the subject of one of the previous inventions.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 37-48: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising MK-0431 and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 37 the one of invention 2 for invention 38, and so on to the one of invention 12 for invention 48, as far as not included in the subject of one of the previous inventions.

Inventions 49-60: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising GSK23A and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 49 the one of invention 2 for invention 50, and so on to the one of invention 12 for invention 60, as far as not included in the subject of one of the previous inventions.

Inventions 61-72: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising BMS-477118 and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 61 the one of invention 2 for invention 62, and so on to the one of invention 12 for invention 72, as far as not included in the subject of one of the previous inventions.

Inventions 73-84: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising
3-(aminomethyl)-2-isobutyl-1-oxo-4-phenyl-1,2-dihydro-6-isoquinolinecarboxamide and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 73 the one of invention 2 for invention 74, and so on to the one of invention 12 for invention 84, as far as not included in the subject of one of the previous inventions.

Inventions 85-96 claims 1-3, 6-12 and 14-16 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A combination comprising 2-{{[3-(aminomethyl)-2-isobutyl-4-phenyl-1-oxo-1,2-dihydro-6-isoquinolyl]oxy}acetamide and an antiobesity agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 85 the one of invention 2 for invention 86, and so on to the one of invention 12 for invention 96, as far as not included in the subject of one of the previous inventions.

Inventions 97-108: claims 1-16 (all partially)

A combination comprising 1-{2-[(5-cyanopyridin-2-yl) amino]ethylamino}acetyl-2(S)-cyano-pyrrolidine dihydrochloride and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 97, the one of invention 2 for invention 98, and so on to the one of invention 12 for invention 120, as far as not included in the subject of one of the previous inventions.

Inventions 109-120: claims 1-16 (all partially)

A combination comprising 1(S)-1-[(3-hydroxy-1-adamantyl) amino]acetyl-2-cyano-pyrrolidine and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 109 the one of invention 2 for invention 110, and so on to the one of invention 12 for invention 120, as far as not included in the subject of one of the previous inventions.

Inventions 121-132: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising L-threo- isoleucylthiazolidine and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 121 the one of invention 2 for invention 122, and so on to the one of invention 12 for invention 132, as far as not included in the subject of one of the previous inventions.

Inventions 133-144: claims 1-3, 6-12 and 14-16 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A combination comprising MK-0431 and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 133 the one of invention 2 for invention 134, and so on to the one of invention 12 for invention 144, as far as not included in the subject of one of the previous inventions.

Inventions 145-156: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising GSK23A and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 145 the one of invention 2 for invention 146, and so on to the one of invention 12 for invention 156, as far as not included in the subject of one of the previous inventions.

Inventions 157-168: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising BMS-477118 and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 157 the one of invention 2 for invention 158, and so on to the one of invention 12 for invention 168, as far as not included in the subject of one of the previous inventions.

Inventions 169-180: claims 1-3, 6-12 and 14-16 (all partially)

A combination comprising
3-(aminomethyl)-2-isobutyl-1-oxo-4-phenyl-1,2-dihydro-6-isoquinolinecarboxamide and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 169 the one of invention 2 for invention 170, and so on to the one of invention 12 for invention 180, as far as not included in the subject of one of the previous inventions.

Inventions 181-192: claims 1-3, 6-12 and 14-16 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A combination comprising 2-{{[3-(aminomethyl)-2-isobutyl-4-phenyl-1-oxo-1,2-dihydro-6-isoquinolyl]oxy}acetamide and an appetite regulating agent or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 181 the one of invention 2 for invention 182, and so on to the one of invention 12 for invention 192, as far as not included in the subject of one of the previous inventions.

Inventions 193-204: claims 7, 10, 11 and 13-16 (all partially)

A combination comprising 1-{2-[(5- cyanopyridin-2-yl) amino] ethylamino} acetyl-2 (S)-cyano-pyrrolidine dihydrochloride and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 193, the one of invention 2 for invention 194, and so on to the one of invention 12 for invention 204, as far as not included in the subject of one of the previous inventions.

Inventions 205-216: claims 7, 10, 11 and 13-16 (all partially)

A combination comprising (S)-1-[(3-hydroxy-1-adamantyl) amino]acetyl-2-cyano-pyrrolidine and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 205, the one of invention 2 for invention 206, and so on to the one of invention 12 for invention 216, as far as not included in the subject of one of the previous inventions.

Inventions 217-228: claims 7, 10 and 16 (all partially)

A combination comprising L-threo- isoleucylthiazolidine and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 217, the one of invention 2 for invention 218, and so on to the one of invention 12 for invention 228, as far as not included in the subject of one of the previous inventions.

Inventions 229-240: claims 7, 10 and 16 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A combination comprising MK-0431 and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 229, the one of invention 2 for invention 230, and so on to the one of invention 12 for invention 240, as far as not included in the subject of one of the previous inventions.

Inventions 241-252: claims 7, 10 and 16 (all partially)

A combination comprising GSK23A and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 241, the one of invention 2 for invention 242, and so on to the one of invention 12 for invention 252, as far as not included in the subject of one of the previous inventions.

Inventions 253-264: claims 7, 10 and 16 (all partially)

A combination comprising BMS-477118 and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 253, the one of invention 2 for invention 254, and so on to the one of invention 12 for invention 264, as far as not included in the subject of one of the previous inventions.

Inventions 265-276: claims 7, 10 and 16 (all partially)

A combination comprising 3-(aminomethyl)-2-isobutyl-1-oxo-4-phenyl-1,2-dihydro-6-isoquinolinecarboxamide and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 265, the one of invention 2 for invention 266, and so on to the one of invention 12 for invention 276, as far as not included in the subject of one of the previous inventions.

Inventions 277-288: claims 7, 10 and 16 (all partially)

A combination comprising 2-{{[3-(aminomethyl)-2-isobutyl-4-phenyl-1-oxo-1,2-dihydro-6-isoquinolyl]oxy}acetamide and a renin inhibitor or a pharmaceutically acceptable salt thereof, for the prevention, or delay of progression, or treatment of a disease selected from the one of invention 1 for invention 277, the one of invention 2 for invention 278, and so on to the one of invention 12 for invention 288, as far as not included in the subject of one of the previous inventions.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/012989

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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